Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1653HXP

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 8	JAN 30	Saved answer limit increased
NEWS 9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 14	FEB 28	TOXCENTER reloaded with enhancements
NEWS 15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16	MAR 01	INSPEC reloaded and enhanced
NEWS 17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18	MAR 08	X.25 communication option no longer available after June 2006
NEWS 19	MAR 22	EMBASE is now updated on a daily basis
NEWS 20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer

agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:55:54 ON 15 APR 2006

=> file medline, biosis

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 12:56:15 ON 15 APR 2006

FILE 'BIOSIS' ENTERED AT 12:56:15 ON 15 APR 2006
Copyright (c) 2006 The Thomson Corporation

=> s smurf and (activity)
L1 13 SMURF AND (ACTIVITY)

=> d l1 ti abs ibib tot

L1 ANSWER 1 OF 13 MEDLINE on STN
TI Regulation of Smurf2 ubiquitin ligase **activity** by anchoring the E2 to the HECT domain.
AB The conjugation of ubiquitin to proteins involves a cascade of activating (E1), conjugating (E2), and ubiquitin-ligating (E3) type enzymes that commonly signal protein destruction. In TGFbeta signaling the inhibitory protein Smad7 recruits Smurf2, an E3 of the C2-WW-HECT domain class, to the TGFbeta receptor complex to facilitate receptor degradation. Here, we demonstrate that the amino-terminal domain (NTD) of Smad7 stimulates **Smurf activity** by recruiting the E2, UbcH7, to the HECT domain. A 2.1 A resolution X-ray crystal structure of the Smurf2 HECT domain reveals that it has a suboptimal E2 binding pocket that could be optimized by mutagenesis to generate a HECT domain that functions independently of Smad7 and potently inhibits TGFbeta signaling. Thus, E2 enzyme recognition by an E3 HECT enzyme is not constitutively competent and provides a point of control for regulating the ubiquitin ligase **activity** through the action of auxiliary proteins.
ACCESSION NUMBER: 2005401565 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16061177
TITLE: Regulation of Smurf2 ubiquitin ligase **activity** by anchoring the E2 to the HECT domain.
AUTHOR: Ogunjimi Abiodun A; Briant Douglas J; Pece-Barbara Nadia; Le Roy Christine; Di Guglielmo Gianni M; Kavsak Peter; Rasmussen Richele K; Seet Bruce T; Sicheri Frank; Wrana Jeffrey L
CORPORATE SOURCE: Programme in Molecular Biology and Cancer, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario M5G 1X5, Canada.
SOURCE: Molecular cell, (2005 Aug 5) Vol. 19, No. 3, pp. 297-308. Journal code: 9802571. ISSN: 1097-2765.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 20050803
Last Updated on STN: 20051103
Entered Medline: 20051101

L1 ANSWER 2 OF 13 MEDLINE on STN
TI NEDD4-2 (neural precursor cell expressed, developmentally down-regulated 4-2) negatively regulates TGF-beta (transforming growth factor-beta) signalling by inducing ubiquitin-mediated degradation of Smad2 and TGF-beta type I receptor.
AB Inhibitory Smad, Smad7, is a potent inhibitor of TGF-beta (transforming growth factor-beta) superfamily signalling. By binding to activated type I receptors, it prevents the activation of R-Smads (receptor-regulated Smads). To identify new components of the Smad pathway, we performed yeast two-hybrid screening using Smad7 as bait, and identified NEDD4-2 (neural precursor cell expressed, developmentally down-regulated 4-2) as a direct binding partner of Smad7. NEDD4-2 is structurally similar to Smurfs (Smad ubiquitin regulatory factors) 1 and 2, which were identified previously as E3 ubiquitin ligases for R-Smads and TGF-beta superfamily receptors. NEDD4-2 functions like Smurfs 1 and 2 in that it associates with TGF-beta type I receptor via Smad7, and induces its ubiquitin-dependent degradation. Moreover, NEDD4-2 bound to TGF-beta-specific R-Smads, Smads 2 and 3, in a ligand-dependent manner, and induced degradation of Smad2, but not Smad3. However, in contrast with Smurf2, NEDD4-2 failed to induce ubiquitination of SnoN (Ski-related novel protein N), although NEDD4-2 bound to SnoN via Smad2 more strongly than Smurf2. We showed further that overexpressed NEDD4-2 prevents transcriptional **activity** induced by TGF-beta and BMP, whereas silencing of the NEDD4-2 gene by siRNA (small interfering RNA) resulted in enhancement of the responsiveness to TGF-beta superfamily cytokines. These data suggest that NEDD4-2 is a member of the **Smurf**-like C2-WW-HECT (WW is Trp-Trp and HECT is homologous to the E6-accessory protein) type E3 ubiquitin ligases, which negatively regulate TGF-beta superfamily signalling through similar, but not identical, mechanisms to those used by Smurfs.
ACCESSION NUMBER: 2005112864 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15496141
TITLE: NEDD4-2 (neural precursor cell expressed, developmentally down-regulated 4-2) negatively regulates TGF-beta (transforming growth factor-beta) signalling by inducing ubiquitin-mediated degradation of Smad2 and TGF-beta type I receptor.
AUTHOR: Kuratomi Go; Komuro Akiyoshi; Goto Kouichiro; Shinozaki Masahiko; Miyazawa Keiji; Miyazono Kohei; Imamura Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research (JFCR), 1-37-1 Kami-ikebukuro, Toshima-ku, Tokyo 170-8455, Japan.
SOURCE: The Biochemical journal, (2005 Mar 15) Vol. 386, No. Pt 3, pp. 461-70.
Journal code: 2984726R. E-ISSN: 1470-8728.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 20050304
Last Updated on STN: 20050826
Entered Medline: 20050825

L1 ANSWER 3 OF 13 MEDLINE on STN
TI Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the

acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation. The extent of the acetylation is up-regulated by the transforming growth factor-beta signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.

ACCESSION NUMBER: 2004349788 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15138260
TITLE: Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AUTHOR: Jin Yun-Hye; Jeon Eun-Joo; Li Qing-Lin; Lee Yong Hee; Choi Joong-Kook; Kim Wun-Jae; Lee Kwang-Youl; Bae Suk-Chul
CORPORATE SOURCE: Department of Biochemistry and Urology, School of Medicine and Institute for Tumor Research, Chungbuk National University, Cheongju 361-763, South Korea.
SOURCE: The Journal of biological chemistry, (2004 Jul 9) Vol. 279, No. 28, pp. 29409-17. Electronic Publication: 2004-05-10. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040716
Last Updated on STN: 20040825
Entered Medline: 20040824

L1 ANSWER 4 OF 13 MEDLINE on STN
TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AB The principal effect of TGF-beta1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-beta loop in the pathogenesis of scleroderma. In this study, we focused on Smad7 and Smurfs, principal molecules in the negative regulation of TGF-beta signaling, to further understand the autocrine TGF-beta loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-beta receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human alpha2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-beta receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-beta receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf**-mediated inhibitory effect on TGF-beta signaling might contribute to maintaining the autocrine TGF-beta loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed negative regulation of TGF-beta signaling in fibrotic disorders.

ACCESSION NUMBER: 2004023363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14722617
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AUTHOR: Asano Yoshihide; Ihn Hironobu; Yamane Kenichi; Kubo Masahide; Tamaki Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, Tokyo, Japan.

SOURCE: The Journal of clinical investigation, (2004 Jan) Vol. 113, No. 2, pp. 253-64.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040115
Last Updated on STN: 20040210
Entered Medline: 20040209

L1 ANSWER 5 OF 13 MEDLINE on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AB Smad ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory Smad (I-Smad) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-Smad in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.
ACCESSION NUMBER: 2003328281 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12857866
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR: Murakami Gyo; Watabe Tetsuro; Takaoka Kunio; Miyazono Kohei; Imamura Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo 170-8455, Japan.
SOURCE: Molecular biology of the cell, (2003 Jul) Vol. 14, No. 7, pp. 2809-17. Electronic Publication: 2003-04-04.
Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20030715
Last Updated on STN: 20040414
Entered Medline: 20040413

L1 ANSWER 6 OF 13 MEDLINE on STN
TI Cell cycle regulatory E3 ubiquitin ligases as anticancer targets.
AB Disregulation of the cell cycle and proliferation play key roles in cellular transformation and tumorigenesis. Such processes are intimately tied to the concentration, localization and **activity** of enzymes, adapters, receptors, and structural proteins in cells. Ubiquitination of these cellular regulatory proteins, governed by specific enzymes in the ubiquitin (Ub) conjugation cascade, has profound effects on their various functions, most commonly through proteasome targeting and degradation. This review will focus on a variety of E3 Ub ligases as potential oncology drug targets, with particular emphasis on the role of these molecules in

the regulation of stability, localization, and **activity** of key proteins such as tumor suppressors and oncoproteins. E3 ubiquitin ligases that have established roles in cell cycle and apoptosis, such as the anaphase-promoting complex (APC), the Skp-1-Cul1-F-box class, and the murine double minute 2 (MDM2) protein, in addition to more recently discovered E3 ubiquitin ligases which may be similarly important in tumorigenesis, (e.g. **Smurf** family, CHFR, and Efp), will be discussed. We will present evidence to support E3 ligases as good biological targets in the development of anticancer therapeutics and address challenges in drug discovery for these targets.

ACCESSION NUMBER: 2003024782 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12531181
TITLE: Cell cycle regulatory E3 ubiquitin ligases as anticancer targets.
AUTHOR: Pray Todd R; Parlati Francesco; Huang Jianing; Wong Brian R; Payan Donald G; Bennett Mark K; Issakani Sarkiz Daniel; Molineaux Susan; Demo Susan D
CORPORATE SOURCE: Rigel Pharmaceuticals, Inc., 240 East Grand Avenue, South San Francisco, California 94080, USA.. tpray@rigel.com
SOURCE: Drug resistance updates : reviews and commentaries in antimicrobial and anticancer chemotherapy, (2002 Dec) Vol. 5, No. 6, pp. 249-58. Ref: 80
Journal code: 9815369. ISSN: 1368-7646.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030118
Last Updated on STN: 20030521
Entered Medline: 20030520

L1 ANSWER 7 OF 13 MEDLINE on STN
TI The hydrostatic and hydrodynamic volumes of polyols in aqueous solutions and their sweet taste.
AB The tastes and solution properties of sugar alcohols were studied in an attempt to illuminate the mechanism of sweet taste chemoreception. The **SMURF** method was used to measure tastetime-intensity of aqueous solutions of sugar alcohols and the results were interpreted using the Stevens power function and kinetic parameters. The apparent molar volumes, apparent specific volumes, partial molar volumes, partial specific volumes and intrinsic viscosities of the solutions were studied. Apparent molar volume reflects the size of the molecule in a hydrostatic state whereas intrinsic viscosity gives a measure of the size of the molecules in a hydrodynamic state. Generally the apparent molar volumes of the polyols are 6-13% greater than those of the parent sugars, indicating less interaction with the water structure. Apparent specific volume values can predict taste quality, and the average apparent specific volume for the sugar alcohols studied fits within the central part of the sweet range, i.e. 0.5-0.68 cm3/g, which accords with their ability to elicit a pure sweet taste response. Intensities and persistences of sweetness in the polyols followed the same trend as intrinsic viscosities.

ACCESSION NUMBER: 97292388 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9146905
TITLE: The hydrostatic and hydrodynamic volumes of polyols in aqueous solutions and their sweet taste.
AUTHOR: Lopez Chavez A; Birch G G
CORPORATE SOURCE: Department of Agriculture & Food Technology, ITESM, Queretaro, Mexico.
SOURCE: Chemical senses, (1997 Apr) Vol. 22, No. 2, pp. 149-61.
Journal code: 8217190. ISSN: 0379-864X.
PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970723

L1 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Regulation of Smurf2 ubiquitin ligase **activity** by anchoring the E2 to the HECT domain.
AB The conjugation of ubiquitin to proteins involves a cas cade of activating (E1), conjugating (E2), and ubiquitinligating (E3) type enzymes that commonly signal protein destruction. In TGF beta signaling the inhibitory protein Smad7 recruits Smurf2, an E3 of the C2-WW-HECT domain class, to the TGF beta receptor complex to facilitate receptor degradation. Here, we demonstrate that the amino-terminal domain (NTD) of Smad7 stimulates **Smurf activity** by recruiting the E2, UbcH7, to the HECT domain. A 2.1 A resolution X-ray crystal structure of the Smurf2 HECT domain reveals that it has a suboptimal E2 binding pocket that could be optimized by mutagenesis to generate a HECT domain that functions independently of Smad7 and potently inhibits TGF beta signaling. Thus, E2 enzyme recognition by an E3 HECT enzyme is not constitutively competent and provides a point of control for regulating the ubiquitin ligase **activity** through the action of auxiliary proteins.
ACCESSION NUMBER: 2005:452686 BIOSIS
DOCUMENT NUMBER: PREV200510240271
TITLE: Regulation of Smurf2 ubiquitin ligase **activity** by anchoring the E2 to the HECT domain.
AUTHOR(S): Ogunjimi, Abiodun A.; Briant, Douglas J.; Pece-Barbara, Nadia; Le Roy, Christine; Di Guglielmo, Glanni M.; Kavsak, Peter; Rasmussen, Richele K.; Seet, Bruce T.; Sicheri, Frank [Reprint Author]; Wrana, Jeffrey L.
CORPORATE SOURCE: Mt Sinai Hosp, Programme Mol Biol, Toronto, ON M5G 1X5, Canada
sicheri@mshri.on.ca; wrana@mshri.on.ca
SOURCE: Molecular Cell, (AUG 5 2005) Vol. 19, No. 3, pp. 297-308. ISSN: 1097-2765.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Nov 2005
Last Updated on STN: 3 Nov 2005

L1 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI NEDD4-2 (neural precursor cell expressed, developmentally down-regulated 4-2) negatively regulates TGF-ss (transforming growth factor-beta) signalling by inducing ubiquitin-mediated degradation of Smad2 and TGF-beta type I receptor.
AB Inhibitory Smad, Smad7, is a potent inhibitor of TGF-beta (transforming growth factor-beta) superfamily signalling. By binding to activated type I receptors, it prevents the activation of R-Smads (receptor-regulated Smads). To identify new components of the Smad pathway, we performed yeast two-hybrid screening using Smad7 as bait, and identified NEDD4-2 (neural precursor cell expressed, developmentally down-regulated 4-2) as a direct binding partner of Smad7. NEDD4-2 is structurally similar to Smurfs (Smad ubiquitin regulatory factors) 1 and 2, which were identified previously as E3 ubiquitin ligases for R-Smads and TGF-beta superfamily receptors. NEDD4-2 functions like Smurfs I and 2 in that it associates with TGF-beta type I receptor via Smad7, and induces its ubiquitin-dependent degradation. Moreover, NEDD4-2 bound to TGF-beta-specific R-Smads, Smads 2 and 3, in a ligand-dependent manner,

and induced degradation of Smad2, but not Smad3. However, in contrast with Smurf2, NEDD4-2 failed to induce ubiquitination of SnoN (Ski-related novel protein N), although NEDD4-2 bound to SnoN via Smad2 more strongly than Smurf2. We showed further that overexpressed NEDD4-2 prevents transcriptional **activity** induced by TGF-beta and BMP, whereas silencing of the NEDD4-2 gene by siRNA (small interfering RNA) resulted in enhancement of the responsiveness to TGF-beta superfamily cytokines. These data suggest that NEDD4-2 is a member of the **Smurf**-like C2-WW-HECT (WW is Trp-Trp and HECT is homologous to the E6-accessory protein) type E3 ubiquitin ligases, which negatively regulate TGF-beta superfamily signalling through similar, but not identical, mechanisms to those used by Smurfs.

ACCESSION NUMBER: 2005:244473 BIOSIS
DOCUMENT NUMBER: PREV200510026231
TITLE: NEDD4-2 (neural precursor cell expressed, developmentally down-regulated 4-2) negatively regulates TGF-ss (transforming growth factor-beta) signalling by inducing ubiquitin-mediated degradation of Smad2 and TGF-beta type I receptor.
AUTHOR(S): Kuratomi, Go; Komuro, Akiyoshi; Goto, Kouichiro; Shinozaki, Masahiko; Miyazawa, Keiji; Miyazono, Kohei [Reprint Author]; Imamura, Takeshi
CORPORATE SOURCE: Japanese Fdn Canc Res, Inst Canc, Dept Biochem, Toshima Ku, 1-37-1 Kami Ikebukuro, Tokyo 170, Japan
miyazono-ind@umin.ac.jp
SOURCE: Biochemical Journal, (MAR 15 2005) Vol. 386, pp. 461-470. ISSN: 0264-6021.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jun 2005
Last Updated on STN: 29 Jun 2005

L1 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation. The extent of the acetylation is up-regulated by the transforming growth factor-beta signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.

ACCESSION NUMBER: 2004:347664 BIOSIS
DOCUMENT NUMBER: PREV200400349524
TITLE: Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AUTHOR(S): Jin, Yun-Hye; Jeon, Eun-Joo; Lin, Qing-; Lee, Yong Hee; Choi, Joong-Kook; Kim, Wun-Jae; Lee, Kwang-Youl [Reprint Author]; Bae, Suk-Chul
CORPORATE SOURCE: Sch MedDept Biochem, Chungbuk Natl Univ, Cheongju, 361763, South Korea
ginsenoside@runx3.co.kr; scbae@med.chungbuk.ac.kr
SOURCE: Journal of Biological Chemistry, (July 9 2004) Vol. 279,

No. 28, pp. 29409-29417. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Aug 2004
Last Updated on STN: 18 Aug 2004

L1 ANSWER 11 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AB The principal effect of TGF-beta1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-beta loop in the pathogenesis of scleroderma. In this study, we focused on Smad7 and Smurfs, principal molecules in the negative regulation of TGF-beta signaling, to further understand the autocrine TGF-beta loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-beta receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human alpha2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-beta receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-beta receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf**-mediated inhibitory effect on TGF-beta signaling might contribute to maintaining the autocrine TGF-beta loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed negative regulation of TGF-beta signaling in fibrotic disorders.
ACCESSION NUMBER: 2004:94938 BIOSIS
DOCUMENT NUMBER: PREV200400084043
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AUTHOR(S): Asano, Yoshihide; Ihn, Hironobu [Reprint Author]; Yamane, Kenichi; Kubo, Masahide; Tamaki, Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-8655, Japan
IN-DER@h.u-tokyo.ac.jp
SOURCE: Journal of Clinical Investigation, (January 2004) Vol. 113, No. 2, pp. 253-264. print.
CODEN: JCINAO. ISSN: 0021-9738.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Feb 2004
Last Updated on STN: 11 Feb 2004

L1 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AB Smad ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory Smad (I-Smad) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-Smad in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not

necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:356072 BIOSIS
DOCUMENT NUMBER: PREV200300356072
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei [Reprint Author]; Imamura, Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (July 2003) Vol. 14, No. 7, pp. 2809-2817. print.
ISSN: 1059-1524 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

L1 ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Specificity and complexity in **Smurf**-mediated Smad degradation.
ACCESSION NUMBER: 2002:133151 BIOSIS
DOCUMENT NUMBER: PREV200200133151
TITLE: Specificity and complexity in **Smurf**-mediated Smad degradation.
AUTHOR(S): Liang, Min [Reprint author]; Lin, Xia [Reprint author]; Liang, Yao-Yun [Reprint author]; Feng, Xin-Hua [Reprint author]; DeBakey, Michael E. [Reprint author]
CORPORATE SOURCE: Department of Surgery, Baylor College of Medicine, One Baylor Plaza, 139D, Houston, TX, 77030, USA
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 148a. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology. Washington DC, USA. December 08-12, 2001. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Feb 2002
Last Updated on STN: 26 Feb 2002

=> d his

(FILE 'HOME' ENTERED AT 12:55:54 ON 15 APR 2006)

FILE 'MEDLINE, BIOSIS' ENTERED AT 12:56:15 ON 15 APR 2006
L1 13 S SMURF AND (ACTIVITY)

=> s (Smurf1 and WW domain)
L2 0 (SMURF1 AND WW DOMAIN)

=> s (Smurf1 and HECT domain)
L3 11 (SMURF1 AND HECT DOMAIN)

=> d l3 ti abs ibib tot

L3 ANSWER 1 OF 11 MEDLINE on STN
TI Degradation of RhoA by **Smurf1** ubiquitin ligase.
AB The Rho family of small GTPases plays a key role in the dynamic regulation of the actin cytoskeleton that underlies various important cellular functions such as shape changes, migration, and polarity. We found that **Smurf1**, a **HECT domain** E3 ubiquitin ligase, could specifically target RhoA but not Cdc42 or Rac1 for degradation. **Smurf1** interacts with the dominant inactive form of RhoA, RhoA N19, which binds constitutively to guanine nucleotide exchange factors (GEFs) in vivo. **Smurf1** also interacts directly with either nucleotide-free or GDP-bound RhoA in vitro; however, loading with GTPgammaS inhibits the interaction. RhoA is ubiquitinated by wild-type **Smurf1** but not the catalytic mutant of **Smurf1** (C699A) in vivo and in vitro, indicating that RhoA is a direct substrate of **Smurf1**. In this chapter, we summarize the systems and methods used in the analyses of **Smurf1**-regulated RhoA ubiquitination and degradation.
ACCESSION NUMBER: 2006087654 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16472676
TITLE: Degradation of RhoA by **Smurf1** ubiquitin ligase.
AUTHOR: Wang Hong-Rui; Ogunjimi Abiodun A; Zhang Yue; Ozdamar Barish; Bose Rohit; Wrana Jeffrey L
CORPORATE SOURCE: Mount Sinai Hospital, University of Toronto, Ontario, Canada.
SOURCE: Methods in enzymology, (2006) Vol. 406, pp. 437-47. Journal code: 0212271. ISSN: 0076-6879.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200603
ENTRY DATE: Entered STN: 20060214
Last Updated on STN: 20060324
Entered Medline: 20060323

L3 ANSWER 2 OF 11 MEDLINE on STN
TI Degradation of the tumor suppressor Smad4 by WW and **HECT domain** ubiquitin ligases.
AB Smad4 mediates signaling by the transforming growth factor-beta (TGF-beta) superfamily of cytokines. Smad signaling is negatively regulated by inhibitory (I) Smads and ubiquitin-mediated processes. Known mechanisms of proteasomal degradation of Smads depend on the direct interaction of specific E3 ligases with Smads. Alternatively, I-Smads elicit degradation of the TGF-beta receptor by recruiting the WW and **HECT domain** E3 ligases, Smurfs, WWP1, or NEDD4-2. We describe an equivalent mechanism of degradation of Smad4 by the above E3 ligases, via formation of ternary complexes between Smad4 and Smurfs, mediated by R-Smads (Smad2) or I-Smads (Smad6/7), acting as adaptors. Smurfs, which otherwise cannot directly bind to Smad4, mediated poly-ubiquitination of Smad4 in the presence of Smad6 or Smad7. Smad4 co-localized with Smad7 and **Smurf1** primarily in the cytoplasm and in peripheral cell protrusions. Smad2 or Smad7 mutants defective in Smad4 interaction failed to induce **Smurf1**-mediated down-regulation of Smad4. A Smad4 mutant defective in Smad2 or Smad7 interaction could not be effectively down-regulated by **Smurf1**. We propose that Smad4 is targeted for degradation by multiple ubiquitin ligases that can simultaneously act on R-Smads and signaling receptors. Such mechanisms of down-regulation of TGF-beta signaling may be critical for proper physiological response to this pathway.
ACCESSION NUMBER: 2005290965 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15817471
TITLE: Degradation of the tumor suppressor Smad4 by WW and

HECT domain ubiquitin ligases.

AUTHOR: Moren Anita; Imamura Takeshi; Miyazono Kohei; Heldin Carl-Henrik; Moustakas Aristidis

CORPORATE SOURCE: Ludwig Institute for Cancer Research, Box 595, Biomedical Center, Uppsala University, SE-751 24 Uppsala, Sweden.

SOURCE: The Journal of biological chemistry, (2005 Jun 10) Vol. 280, No. 23, pp. 22115-23. Electronic Publication: 2005-04-06.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200508

ENTRY DATE: Entered STN: 20050607
Last Updated on STN: 20050803
Entered Medline: 20050802

L3 ANSWER 3 OF 11 MEDLINE on STN

TI Ubiquitin ligase **Smurf1** controls osteoblast activity and bone homeostasis by targeting MEKK2 for degradation.

AB Bone is constantly resorbed and formed throughout life by coordinated actions of osteoclasts and osteoblasts. Here we show that **Smurf1**, a **HECT domain** ubiquitin ligase, has a specific physiological role in suppressing the osteogenic activity of osteoblasts. **Smurf1**-deficient mice are born normal but exhibit an age-dependent increase of bone mass. The cause of this increase can be traced to enhanced activities of osteoblasts, which become sensitized to bone morphogenesis protein (BMP) in the absence of **Smurf1**. However, loss of **Smurf1** does not affect the canonical Smad-mediated intracellular TGFbeta or BMP signaling; instead, it leads to accumulation of phosphorylated MEKK2 and activation of the downstream JNK signaling cascade. We demonstrate that **Smurf1** physically interacts with MEKK2 and promotes the ubiquitination and turnover of MEKK2. These results indicate that **Smurf1** negatively regulates osteoblast activity and response to BMP through controlling MEKK2 degradation.

ACCESSION NUMBER: 2005186957 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15820682

TITLE: Ubiquitin ligase **Smurf1** controls osteoblast activity and bone homeostasis by targeting MEKK2 for degradation.

AUTHOR: Yamashita Motozo; Ying Sai-Xia; Zhang Gen-Mu; Li Cuiling; Cheng Steven Y; Deng Chu-Xia; Zhang Ying E

CORPORATE SOURCE: Laboratory of Cellular and Molecular Biology, Center for Cancer Research, National Cancer Institute, Bethesda, Maryland 20892, USA.

SOURCE: Cell, (2005 Apr 8) Vol. 121, No. 1, pp. 101-13.
Journal code: 0413066. ISSN: 0092-8674.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200506

ENTRY DATE: Entered STN: 20050412
Last Updated on STN: 20050614
Entered Medline: 20050613

L3 ANSWER 4 OF 11 MEDLINE on STN

TI Bone morphogenetic proteins.

AB Bone morphogenetic proteins (BMPs) are multi-functional growth factors that belong to the transforming growth factor beta (TGFbeta) superfamily. The roles of BMPs in embryonic development and cellular functions in postnatal and adult animals have been extensively studied in recent years.

Signal transduction studies have revealed that Smad1, 5 and 8 are the immediate downstream molecules of BMP receptors and play a central role in BMP signal transduction. Studies from transgenic and knockout mice and from animals and humans with naturally occurring mutations in BMPs and related genes have shown that BMP signaling plays critical roles in heart, neural and cartilage development. BMPs also play an important role in postnatal bone formation. BMP activities are regulated at different molecular levels. Preclinical and clinical studies have shown that BMP-2 can be utilized in various therapeutic interventions such as bone defects, non-union fractures, spinal fusion, osteoporosis and root canal surgery. Tissue-specific knockout of a specific BMP ligand, a subtype of BMP receptors or a specific signaling molecule is required to further determine the specific role of a BMP ligand, receptor or signaling molecule in a particular tissue. BMPs are members of the TGFbeta superfamily. The activity of BMPs was first identified in the 1960s (Urist, M.R. (1965) "Bone formation by autoinduction", Science 150, 893-899), but the proteins responsible for bone induction remained unknown until the purification and sequence of bovine BMP-3 (osteogenin) and cloning of human BMP-2 and 4 in the late 1980s (Wozney, J.M. et al. (1988) "Novel regulators of bone formation: molecular clones and activities", Science 242, 1528-1534; Luyten, F.P. et al. (1989) "Purification and partial amino acid sequence of osteogenin, a protein initiating bone differentiation", J. Biol. Chemical 264, 13377-13380; Wozney, J.M. (1992) "The bone morphogenetic protein family and osteogenesis", Mol. Reprod. Dev. 32, 160-167). To date, around 20 BMP family members have been identified and characterized. BMPs signal through serine/threonine kinase receptors, composed of type I and II subtypes. Three type I receptors have been shown to bind BMP ligands, type IA and IB BMP receptors (BMPR-IA or ALK-3 and BMPR-IB or ALK-6) and type IA activin receptor (ActR-IA or ALK-2) (Koenig, B.B. et al. (1994) "Characterization and cloning of a receptor for BMP-2 and BMP-4 from NIH 3T3 cells", Mol. Cell. Biol. 14, 5961-5974; ten Dijke, P. et al. (1994) "Identification of type I receptors for osteogenic protein-1 and bone morphogenetic protein-4", J. Biol. Chemical 269, 16985-16988; Macias-Silva, M. et al. (1998) "Specific activation of Smad1 signaling pathways by the BMP7 type I receptor, ALK2", J. Biol. Chemical 273, 25628-25636). Three type II receptors for BMPs have also been identified and they are type II BMP receptor (BMPR-II) and type II and IIB activin receptors (ActR-II and ActR-IIB) (Yamashita, H. et al. (1995) "Osteogenic protein-1 binds to activin type II receptors and induces certain activin-like effects", J. Cell. Biol. 130, 217-226; Rosenzweig, B.L. et al. (1995) "Cloning and characterization of a human type II receptor for bone morphogenetic proteins", Proc. Natl Acad. Sci. USA 92, 7632-7636; Kawabata, M. et al. (1995) "Cloning of a novel type II serine/threonine kinase receptor through interaction with the type I transforming growth factor-beta receptor", J. Biol. Chemical 270, 5625-5630). Whereas BMPR-IA, IB and II are specific to BMPs, ActR-IA, II and IIB are also signaling receptors for activins. These receptors are expressed differentially in various tissues. Type I and II BMP receptors are both indispensable for signal transduction. After ligand binding they form a heterotetrameric-activated receptor complex consisting of two pairs of a type I and II receptor complex (Moustakas, A. and C.H. Heldi (2002) "From mono- to oligo-Smads: the heart of the matter in TGFbeta signal transduction" Genes Dev. 16, 67-871). The type I BMP receptor substrates include a protein family, the Smad proteins, that play a central role in relaying the BMP signal from the receptor to target genes in the nucleus. Smad1, 5 and 8 are phosphorylated by BMP receptors in a ligand-dependent manner (Hoodless, P.A. et al. (1996) "MADR1, a MAD-related protein that functions in BMP2 signaling pathways", Cell 85, 489-500; Chen Y. et al. (1997) "Smad8 mediates the signaling of the receptor serine kinase", Proc. Natl Acad. Sci. USA 94, 12938-12943; Nishimura R. et al. (1998) "Smad5 and DPC4 are key molecules in mediating BMP-2-induced osteoblastic differentiation of the pluripotent mesenchymal precursor cell line C2C12", J. Biol. Chemical 273, 1872-1879). After release from the receptor, the

phosphorylated Smad proteins associate with the related protein Smad4, which acts as a shared partner. This complex translocates into the nucleus and participates in gene transcription with other transcription factors (). A significant advancement about the understanding of in vivo functions of BMP ligands, receptors and signaling molecules has been achieved in recent years. <figgrp> <title>Figure 1 BMP signaling and its regulation. BMP signals are mediated by type I and II BMP receptors and their downstream molecules Smad1, 5 and 8. Phosphorylated Smad1, 5 and 8 proteins form a complex with Smad4 and then are translocated into the nucleus where they interact with other transcription factors, such as Runx2 in osteoblasts. BMP signaling is regulated at different molecular levels: (1) Noggin and other cystine knot-containing BMP antagonists bind with BMP-2, 4 and 7 and block BMP signaling. Over-expression of noggin in mature osteoblasts causes osteoporosis in mice (<citeref rid="bib9">Devlin et al., 2003</citeref>; <citeref rid="bib65">Wu et al., 2003</citeref>). (2) Smad6 binds type I BMP receptor and prevents Smad1, 5 and 8 to be activated (<citeref rid="bib22">Imamura et al., 1997</citeref>). Over-expression of Smad6 in chondrocytes causes delays in chondrocyte differentiation and maturation (<citeref rid="bib21">Horiki et al., 2004</citeref>). (3) Tob interacts specifically with BMP activated Smad proteins and inhibits BMP signaling. In Tob null mutant mice, BMP signaling is enhanced and bone formation is increased (<citeref rid="bib71">Yoshida et al., 2000</citeref>). (4) **Smurf1** is a **Hect domain** E3 ubiquitin ligase. It interacts with Smad1 and 5 and mediates the degradation of these Smad proteins (<citeref rid="bib76">Zhu et al., 1999</citeref>). (5) **Smurf1** also recognizes bone-specific transcription factor Runx2 and mediates Runx2 degradation (<citeref rid="bib74">Zhao et al., 2003</citeref>). (6) **Smurf1** also forms a complex with Smad6, is exported from the nucleus and targeted to the type I BMP receptors for their degradation (<citeref rid="bib40">Murakami et al., 2003</citeref>). Over-expression of **Smurf1** in osteoblasts inhibits postnatal bone formation in mice (<citeref rid="bib75">Zhao et al., 2004</citeref>).</title> <fig id="fig1" name="GGRF0233fig001"></fig> </figgrp>

ACCESSION NUMBER: 2004644770 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15621726
TITLE: Bone morphogenetic proteins.
AUTHOR: Chen Di; Zhao Ming; Mundy Gregory R
CORPORATE SOURCE: School of Medicine and Dentistry, Department of Orthopaedics, University of Rochester, Rochester, NY 14642, USA.
SOURCE: Growth factors (Chur, Switzerland), (2004 Dec) Vol. 22, No. 4, pp. 233-41. Ref: 77
Journal code: 9000468. ISSN: 0897-7194.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20041229
Last Updated on STN: 20050520
Entered Medline: 20050519

L3 ANSWER 5 OF 11 MEDLINE on STN
TI **Smurf1**: a link between cell polarity and ubiquitination.
AB Members of the Rho family of small guanosine triphosphatases are well known for their important functions in the dynamic regulation of actin cytoskeleton. We recently found that a **HECT domain** E3 ubiquitin ligase, called **Smurf1**, regulates cell polarity and protrusion formation by targeting RhoA for degradation at cellular protrusions. **Smurf1** regulates these functions as a partner of protein kinase Cxi, a component of the polarity complex. Furthermore,

using siRNA-mediated knockdown, we demonstrated this pathway is required to maintain the transformed morphology and motility of a tumor cell. **Smurf1** thus provides a link between the control of cell polarity and ubiquitin-mediated RhoA degradation during directional cell movements. Here we further discuss the mechanism by which the spatial control of **Smurf1** activity is accomplished and the potential implications of these findings in cancer and development.

ACCESSION NUMBER: 2004387632 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14752271
TITLE: **Smurf1**: a link between cell polarity and ubiquitination.
AUTHOR: Zhang Yue; Wang Hong-Rui; Wrana Jefferey L
CORPORATE SOURCE: Program in Molecular Biology and Cancer, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Canada.
SOURCE: Cell cycle (Georgetown, Tex.), (2004 Apr) Vol. 3, No. 4, pp. 391-2. Electronic Publication: 2004-04-01. Journal code: 101137841. ISSN: 1538-4101.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040805
Last Updated on STN: 20040929
Entered Medline: 20040928

L3 ANSWER 6 OF 11 MEDLINE on STN
TI **Smurf1** inhibits osteoblast differentiation and bone formation in vitro and in vivo.
AB Bone morphogenetic proteins (BMPs) are required for normal postnatal bone formation and osteoblast differentiation. There is evidence from recent studies that BMP signaling in osteoblasts is controlled by an ubiquitin-proteasome regulatory mechanism involving a cascade of enzymatic reactions. The specificity of protein ubiquitination is determined by E3 ubiquitin ligases, which play a crucial role in defining substrate specificity and subsequent protein degradation by 26S proteasomes. We have examined the role of the E3 ubiquitin ligase Smad ubiquitin regulatory factor 1 (**Smurf1**), a member of the **Hect domain** family of E3 ubiquitin ligases in osteoblast function. **Smurf1** has been found to interact with BMP-activated Smad1 and -5 and to mediate degradation of these Smad proteins. Recently we have found that **Smurf1** mediates the protein degradation of the osteoblast-specific transcription factor Runx2/Cbfa1. To determine the role of **Smurf1** in osteoblast differentiation, in the present studies we transfected a **Smurf1** expression plasmid into 2T3 osteoblast precursor cells and found that **Smurf1** overexpression inhibits BMP signaling and osteoblast differentiation. To further investigate the role of **Smurf1** in bone formation in vivo, we generated transgenic mice in which expression of the epitope-tagged **Smurf1** transgene was targeted to osteoblasts using the murine 2.3-kb osteoblast-specific type I collagen promoter. In these transgenic mice, bone formation was significantly reduced during postnatal life. Our results demonstrate for the first time that **Smurf1** plays a specific role in osteoblast differentiation and bone formation in vivo.

ACCESSION NUMBER: 2004141081 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14701828
TITLE: **Smurf1** inhibits osteoblast differentiation and bone formation in vitro and in vivo.
AUTHOR: Zhao Ming; Qiao Mei; Harris Stephen E; Oyajobi Babatunde O; Mundy Gregory R; Chen Di
CORPORATE SOURCE: Department of Cellular and Structural Biology, University of Texas Health Science Center, San Antonio, TX 78229, USA.
CONTRACT NUMBER: AR 048920 (NIAMS)

AR 051189 (NIAMS)
SOURCE: The Journal of biological chemistry, (2004 Mar 26) Vol. 279, No. 13, pp. 12854-9. Electronic Publication: 2003-12-29.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040323
Last Updated on STN: 20040510
Entered Medline: 20040507

L3 ANSWER 7 OF 11 MEDLINE on STN
TI Regulation of cell polarity and protrusion formation by targeting RhoA for degradation.
AB The Rho family of small guanosine triphosphatases regulates actin cytoskeleton dynamics that underlie cellular functions such as cell shape changes, migration, and polarity. We found that **Smurf1**, a **HECT domain** E3 ubiquitin ligase, regulated cell polarity and protrusive activity and was required to maintain the transformed morphology and motility of a tumor cell. Atypical protein kinase C zeta (PKCzeta), an effector of the Cdc42/Rac1-PAR6 polarity complex, recruited **Smurf1** to cellular protrusions, where it controlled the local level of RhoA. **Smurf1** thus links the polarity complex to degradation of RhoA in lamellipodia and filopodia to prevent RhoA signaling during dynamic membrane movements.
ACCESSION NUMBER: 2003577679 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14657501
TITLE: Regulation of cell polarity and protrusion formation by targeting RhoA for degradation.
AUTHOR: Wang Hong-Rui; Zhang Yue; Ozdamar Barish; Ogunjimi Abiodun A; Alexandrova Evguenia; Thomsen Gerald H; Wrana Jeffrey L
CORPORATE SOURCE: Program in Molecular Biology and Cancer, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto M56 1x5, Canada.
CONTRACT NUMBER: HD32429 (NICHD)
SOURCE: Science, (2003 Dec 5) Vol. 302, No. 5651, pp. 1775-9.
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20031230
Entered Medline: 20031229

L3 ANSWER 8 OF 11 MEDLINE on STN
TI The DSmurf ubiquitin-protein ligase restricts BMP signaling spatially and temporally during Drosophila embryogenesis.
AB We identified Drosophila Smurf (DSmurf) as a negative regulator of signaling by the BMP2/4 ortholog DPP during embryonic dorsal-ventral patterning. DSmurf encodes a **HECT domain** ubiquitin-protein ligase, homologous to vertebrate **Smurf1** and Smurf2, that binds the Smad1/5 ortholog MAD and likely promotes its proteolysis. The essential function of DSmurf is restricted to its action on the DPP pathway. DSmurf has two distinct, possibly mechanistically separate, functions in controlling DPP signaling. Prior to gastrulation, DSmurf mutations cause a spatial increase in the DPP gradient, as evidenced by ventrolateral expansion in expression domains of target genes representing all known signaling thresholds. After gastrulation, DSmurf

mutations cause a temporal delay in downregulation of earlier DPP signals, resulting in a lethal defect in hindgut organogenesis.

ACCESSION NUMBER: 2001654271 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11703946
TITLE: The DSmurf ubiquitin-protein ligase restricts BMP signaling spatially and temporally during Drosophila embryogenesis.
AUTHOR: Podos S D; Hanson K K; Wang Y C; Ferguson E L
CORPORATE SOURCE: Department of Molecular Genetics and Cell Biology, University of Chicago, Illinois 60637, USA.
CONTRACT NUMBER: GM50838 (NIGMS)
HD07959 (NICHD)
SOURCE: Developmental cell, (2001 Oct) Vol. 1, No. 4, pp. 567-78. Journal code: 101120028. ISSN: 1534-5807.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF416571
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011115
Last Updated on STN: 20030304
Entered Medline: 20011207

L3 ANSWER 9 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Degradation of the tumor suppressor Smad4 by WW and **HECT domain** ubiquitin ligases.
AB Smad4 mediates signaling by the transforming growth factor-beta (TGF-beta) superfamily of cytokines. Smad signaling is negatively regulated by inhibitory (I) Smads and ubiquitin-mediated processes. Known mechanisms of proteasomal degradation of Smads depend on the direct interaction of specific E3 ligases with Smads. Alternatively, I-Smads elicit degradation of the TGF-beta receptor by recruiting the WW and **HECT domain** E3 ligases, Smurfs, WWP1, or NEDD4-2. We describe an equivalent mechanism of degradation of Smad4 by the above E3 ligases, via formation of ternary complexes between Smad4 and Smurfs, mediated by R-Smads (Smad2) or I-Smads (Smad6/7), acting as adaptors. Smurfs, which otherwise cannot directly bind to Smad4, mediated polyubiquitination of Smad4 in the presence of Smad6 or Smad7. Smad4 co-localized with Smad7 and **Smurf1** primarily in the cytoplasm and in peripheral cell protrusions. Smad2 or Smad7 mutants defective in Smad4 interaction failed to induce **Smurf1**-mediated down-regulation of Smad4. A Smad4 mutant defective in Smad2 or Smad7 interaction could not be effectively down-regulated by **Smurf1**. We propose that Smad4 is targeted for degradation by multiple ubiquitin ligases that can simultaneously act on R-Smads and signaling receptors. Such mechanisms of down-regulation of TGF-beta signaling may be critical for proper physiological response to this pathway.

ACCESSION NUMBER: 2005:348579 BIOSIS
DOCUMENT NUMBER: PREV200510138583
TITLE: Degradation of the tumor suppressor Smad4 by WW and **HECT domain** ubiquitin ligases.
AUTHOR(S): Moren, Anita; Imamura, Takeshi; Miyazono, Kohei; Heldin, Carl-Henrik; Moustakas, Aristidis [Reprint Author]
CORPORATE SOURCE: Uppsala Univ, Biomed Ctr, Ludwig Inst Canc Res, Box 595, SE-75124 Uppsala, Sweden
aris.moustakas@licr.uu.se
SOURCE: Journal of Biological Chemistry, (JUN 10 2005) Vol. 280, No. 23, pp. 22115-22123.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Sep 2005
Last Updated on STN: 8 Sep 2005

L3 ANSWER 10 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

TI Ubiquitin ligase **Smurf1** controls osteoblast activity and bone homeostasis by targeting MEKK2 for degradation.

AB Bone is constantly resorbed and formed throughout life by coordinated actions of osteoclasts and osteoblasts. Here we show that **Smurf1**, a **HECT domain** ubiquitin ligase, has a specific physiological role in suppressing the osteogenic activity of osteoblasts. **Smurf1**-deficient mice are born normal but exhibit an age-dependent increase of bone mass. The cause of this increase can be traced to enhanced activities of osteoblasts, which become sensitized to bone morphogenesis protein (BMP) in the absence of **Smurf1**. However, loss of **Smurf1** does not affect the canonical Smad-mediated intracellular TGF beta or BMP signaling; instead, it leads to accumulation of phosphorylated MEKK2 and activation of the downstream JNK signaling cascade. We demonstrate that **Smurf1** physically interacts with MEKK2 and promotes the ubiquitination and turnover of MEKK2. These results indicate that **Smurf1** negatively regulates osteoblast activity and response to BMP through controlling MEKK2 degradation.

ACCESSION NUMBER: 2005:259633 BIOSIS
DOCUMENT NUMBER: PREV200510044740
TITLE: Ubiquitin ligase **Smurf1** controls osteoblast activity and bone homeostasis by targeting MEKK2 for degradation.
AUTHOR(S): Yamashita, Motozo; Ying, Sai-Xia; Zhang, Gen-mu; Li, Cuiling; Cheng, Steven Y.; Deng, Chu-xia; Zhang, Ying E. [Reprint Author]
CORPORATE SOURCE: NCI, Cellular and Mol Biol Lab, Ctr Canc Res, Bldg 37, Bethesda, MD 20892 USA
yingz@helix.nih.gov
SOURCE: Cell, (APR 8 2005) Vol. 121, No. 1, pp. 101-113.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jul 2005
Last Updated on STN: 14 Jul 2005

L3 ANSWER 11 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

TI Regulation of cell polarity and protrusion formation by targeting RhoA for degradation.

AB The Rho family of small guanosine triphosphatases regulates actin cytoskeleton dynamics that underlie cellular functions such as cell shape changes, migration, and polarity. We found that **Smurf1**, a **HECT domain** E3 ubiquitin ligase, regulated cell polarity and protrusive activity and was required to maintain the transformed morphology and motility of a tumor cell. Atypical protein kinase C zeta (PKCzeta), an effector of the Cdc42/Rac1-PAR6 polarity complex, recruited **Smurf1** to cellular protrusions, where it controlled the local level of RhoA. **Smurf1** thus links the polarity complex to degradation of RhoA in lamellipodia and filopodia to prevent RhoA signaling during dynamic membrane movements.

ACCESSION NUMBER: 2004:31109 BIOSIS
DOCUMENT NUMBER: PREV200400023694
TITLE: Regulation of cell polarity and protrusion formation by targeting RhoA for degradation.
AUTHOR(S): Wang, Hong-rui; Zhang, Yue; Ozdamar, Barish; Ogunjimi, Abiodun A.; Alexandrova, Evguenia; Thomsen, Gerald H.; Wrana, Jeffrey L. [Reprint Author]
CORPORATE SOURCE: Program in Molecular Biology and Cancer, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, M56 1X5, Canada

wrana@mshri.on.ca
SOURCE: Science (Washington D C), (5 December 2003) Vol. 302, No. 5651, pp. 1775-1779. print.
ISSN: 0036-8075 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Dec 2003
Last Updated on STN: 31 Dec 2003

Refine Search

Search Results -

Terms	Documents
Smurf1	5

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L6

Refine Search

Recall Text | Clear | Interrupt

Search History

DATE: Saturday, April 15, 2006 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=OR			
L6	Smurf1	5	L6
L5	L3 and l2	0	L5
L4	L3 and l1	0	L4
L3	thomsen.in.	695	L3
L2	smurf and (WW domain)	5	L2
L1	smurf and (HECT domain)	5	L1

END OF SEARCH HISTORY

Hit List

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

First Hit

Search Results - Record(s) 1 through 5 of 5 returned.

☐ 1. Document ID: US 6912700 B1

L1: Entry 1 of 5 File: USPT Jun 28, 2005

US-PAT-NO: 6912700
DOCUMENT-IDENTIFIER: US 6912700 B1

TITLE: Method and system for non-linear state based satisfiability

DATE-ISSUED: June 28, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Franco; John V.	Cincinnati	OH		
VanFleet; W. Mark	Glen Burnie	MD		
Schlipf; John	Cincinnati	OH		
Dransfield; Michael R.	Ellicott City	MD		

US-CL-CURRENT: 716/5; 703/16, 706/13, 706/16, 706/33, 706/45, 716/18, 716/2, 716/3, 716/7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Ima

☐ 2. Document ID: US 6901517 B1

L1: Entry 2 of 5 File: USPT May 31, 2005

US-PAT-NO: 6901517
DOCUMENT-IDENTIFIER: US 6901517 B1

TITLE: Hardware based security groups, firewall load sharing, and firewall redundancy

DATE-ISSUED: May 31, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Redmore; Seth	Palo Alto	CA		

US-CL-CURRENT: 726/11; 370/252, 717/101

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Ima

☐ 3. Document ID: US 6775657 B1

L1: Entry 3 of 5 File: USPT Aug 10, 2004

US-PAT-NO: 6775657
DOCUMENT-IDENTIFIER: US 6775657 B1

TITLE: Multilayered intrusion detection system and method

DATE-ISSUED: August 10, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Baker; Stephen M.	San Antonio	TX		

US-CL-CURRENT: 706/45; 706/50, 726/22

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Ima

---

☐ 4. Document ID: US 6687247 B1

L1: Entry 4 of 5 File: USPT Feb 3, 2004

US-PAT-NO: 6687247
DOCUMENT-IDENTIFIER: US 6687247 B1

TITLE: Architecture for high speed class of service enabled linecard

DATE-ISSUED: February 3, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wilford; Bruce	Los Altos	CA		
Dan; Yie-Fong	Cupertino	CA		

US-CL-CURRENT: 370/392; 370/412

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Ima

---

☐ 5. Document ID: US 6684250 B2

L1: Entry 5 of 5 File: USPT Jan 27, 2004

US-PAT-NO: 6684250
DOCUMENT-IDENTIFIER: US 6684250 B2

TITLE: Method and apparatus for estimating a geographic location of a networked entity

DATE-ISSUED: January 27, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Anderson; Mark	Westminster	CO		
Bansal; Ajay	Cupertino	CA		
Doctor; Brad	Broomfield	CO		
Hadjiyiannis; George	Boston	MA		
Herringshaw; Christopher	West Wardsboro	VT		
Karplus; Eli E.	Baden Wurttemberg			DE
Muniz; Derald	Midlothian	TX		

US-CL-CURRENT: 709/225; 370/392, 709/228

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Terms	Documents
smurf and (HECT domain)	5

Display Format: CIT Change Format

Previous Page Next Page Go to Doc#

Hit List

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

First Hit

Search Results - Record(s) 1 through 5 of 5 returned.

☐ 1. Document ID: US 7022493 B2

L6: Entry 1 of 5 File: USPT Apr 4, 2006

US-PAT-NO: 7022493
DOCUMENT-IDENTIFIER: US 7022493 B2

TITLE: Ubiquitin conjugation assays

DATE-ISSUED: April 4, 2006

PRIOR-PUBLICATION:

DOC-ID	DATE
US 20050032139 A1	February 10, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Issakani; Sarkiz D.	San Jose	CA		US
Huang; Jianing	Foster City	CA		US
Sheung; Julie	San Francisco	CA		US
Pray; Todd R.	San Francisco	CA		US

US-CL-CURRENT: 435/7.92; 435/14, 435/21, 435/28, 435/7.1, 435/7.4, 435/7.6, 435/7.9, 435/7.91, 435/7.93, 435/7.94, 435/7.95, 436/164, 436/172, 436/544, 436/546, 436/805

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw Desc | Ima

☐ 2. Document ID: US 6979551 B2

L6: Entry 2 of 5 File: USPT Dec 27, 2005

US-PAT-NO: 6979551
DOCUMENT-IDENTIFIER: US 6979551 B2

TITLE: Assays for identifying ubiquitin agents and for identifying agents that modify the activity of ubiquitin agents

DATE-ISSUED: December 27, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Issakani; Sarkiz D.	San Jose	CA		
Huang; Jianing	Foster City	CA		
Sheung; Julie	San Francisco	CA		
Pray; Todd R.	San Francisco	CA		

US-CL-CURRENT: 435/7.92; 435/14, 435/21, 435/28, 435/7.1, 435/7.4, 435/7.6, 435/7.9, 435/7.91, 435/7.93, 435/7.94, 435/7.95, 436/164, 436/172, 436/544, 436/546, 436/805

☐ 3. Document ID: US 6919184 B2

L6: Entry 3 of 5 File: USPT Jul 19, 2005

US-PAT-NO: 6919184
DOCUMENT-IDENTIFIER: US 6919184 B2

TITLE: Assays for identifying ubiquitin agents and for identifying agents that modify the activity of ubiquitin agents

DATE-ISSUED: July 19, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Issakani; Sarkiz D.	San Jose	CA		
Huang; Jianing	Foster City	CA		
Sheung; Julie	San Francisco	CA		
Pray; Todd R.	San Francisco	CA		

US-CL-CURRENT: 435/7.92; 435/14, 435/21, 435/28, 435/7.1, 435/7.4, 435/7.6, 435/7.9, 435/7.91, 435/7.93, 435/7.94, 435/7.95, 436/164, 436/172, 436/544, 436/546, 436/805

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Ima

☐ 4. Document ID: US 6740495 B1

L6: Entry 4 of 5 File: USPT May 25, 2004

US-PAT-NO: 6740495
DOCUMENT-IDENTIFIER: US 6740495 B1
**** See image for Certificate of Correction ****

TITLE: Ubiquitin ligase assay

DATE-ISSUED: May 25, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Issakani; Sarkiz D.	San Jose	CA		
Huang; Jianing	Foster City	CA		
Sheung; Julie	San Francisco	CA		

US-CL-CURRENT: 435/7.92; 435/14, 435/21, 435/28, 435/29, 435/320.1, 435/325, 435/7.1, 435/7.4, 435/7.6, 435/7.9, 435/7.91, 435/7.95, 436/164, 436/172, 436/544, 436/546, 436/805, 536/23.1, 536/23.2, 536/23.5, 536/24.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Ima

☐ 5. Document ID: US 6737244 B2

L6: Entry 5 of 5 File: USPT May 18, 2004

US-PAT-NO: 6737244
DOCUMENT-IDENTIFIER: US 6737244 B2

** See image for Certificate of Correction **

TITLE: Ubiquitin ligase assay

DATE-ISSUED: May 18, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Issakani; Sarkiz D.	San Jose	CA		
Huang; Jianing	Foster City	CA		
Sheung; Julie	San Francisco	CA		
Pray; Todd R.	San Francisco	CA		

US-CL-CURRENT: 435/7.92; 435/14, 435/21, 435/28, 435/7.1, 435/7.4, 435/7.6, 435/7.9, 435/7.91, 435/7.93, 435/7.94, 435/7.95, 436/164, 436/172, 436/544, 436/546, 436/805

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Terms	Documents
Smurf1	5

Display Format: CIT Change Format

Previous Page Next Page Go to Doc#